

Cancer Research Collaborations with the European Union

Douglas R. Lowy, M.D., NCI

Joint NCAB/BSA meeting

June 14, 2023



Goals

- Reduce the cancer death rate by 50% in the next 25 years (in the U.S.)
- Overcome cancer disparities
- End cancer as we know it



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Opportunities for Achieving the Cancer Moonshot Goal of a 50% Reduction in Cancer Mortality by 2047

Meredith S. Shiels, Stanley Lipkowitz, Nicole G. Campos, Mark Schiffman, John T. Schiller, Neal D. Freedman, Amy Berrington de González

TO ACHIEVE THE
CANCER MOONSHOT GOAL

**CANCER DEATH RATES
MUST DECLINE FASTER**



SOURCE: Shiels M, et al. *Cancer Discovery*. 2023.

National Cancer Plan

NationalCancerPlan.cancer.gov

National Cancer Plan



Everyone has a role.

April 3, 2023

U.S. Department of Health & Human Services | National Institutes of Health | National Cancer Institute

National Cancer Plan



*Describes goals, strategies,
and actions needed to end
cancer as we know it*

- **Long-term vision** for ending cancer as we know it
- **A framework for collaboration**
- **All-of-government** approach
- **All-of-society** approach
- **Inclusive of everyone**
(organizations and individuals)
- *Not* a medium-term strategic/action plan
- *Not* confined to research – includes care, advocacy, policy, individual behaviors

Learn more: NationalCancerPlan.cancer.gov

Europe's Beating Cancer Plan and the U.S. Cancer Moonshot: Similar Goals



Similar goals:

- Reduce cancer mortality and reduce disparities
- The reignited Cancer Moonshot places these goals front and center

No one can solve cancer alone.

Ways to work together:

- Collaborative research
- Help support research and cancer control in LMICs

NCI CCDI Coordinated National Initiative for Rare Cancers in Children and Young Adults: Need for International Collaboration

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Rare Cancers Definition and Challenges

- **Definition:** Fewer than <40,000 people/year in US
 - 25% of all adult cancers
 - All pediatric cancers (approximately 20,000/year ages 0-19 years old)
- **Very rare pediatric cancer:**
 - Fewer than 2 cases per million per year (11% of all pediatric cancers)
 - Tumors not considered in clinical trials; lack of standard of care
 - Definition in molecular era:
 - ALK mutated neuroblastoma 1 case/million/year
 - NTRK fusion cancers pediatrics: 1-3 cases/million/year
 - Frequently multiple histologies
- **Challenges:**
 - Accurate and timely diagnosis
 - Poor understanding of natural history and biology
 - Lack of meaningful preclinical models
 - Clinical trials generally not feasible

Rare Disease: Diagnosis and Treatment Odyssey

12y F presenting with neck stiffness

Progressive symptoms

Referral to specialized center



6 m
8 m

How can we better achieve timely and accurate diagnosis and connection with disease experts?

Started standard therapy
After 3 cycles, no response

Diagnosis changed to
poorly differentiated chordoma



Surgery
Proton RT

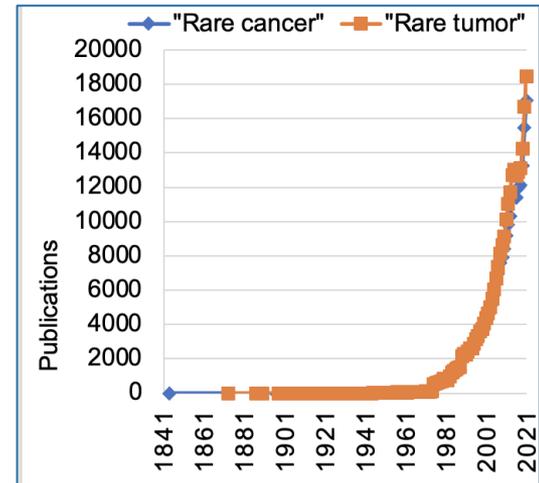
4 years later

Follow up included only imaging
the primary site

Pediatric and AYA Rare Cancer Efforts

- **Children's Oncology Group:** Interventional international trials
 - RB, NPC, ACC, HCC, PPB, ATRT
- **Observational and biology studies:**
 - International Pleuropulmonary Blastoma / DICER1 Registry
 - My Pediatric and Adult Rare Tumor Network (MyPART)
 - European ExPERT/PARTNER Consortium
 - Retrospective reviews
 - Consensus treatment recommendations
 - Tumor boards (disease champions)
- **Limitations:**
 - Focus on few cancers
 - Siloed
 - Insufficient patient numbers for most cancers
 - Data collection limited not standardized/structured

Rare tumor/cancer publications



Why International Collaboration?

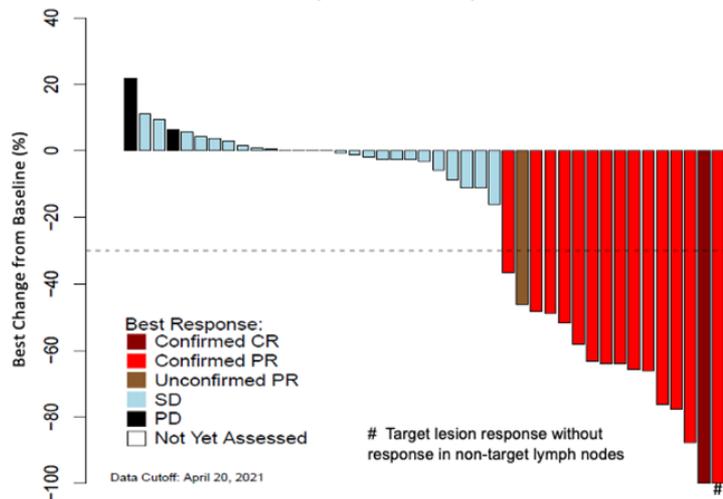
Diagnosis	Incidence	US Patients/Yr	APEC Accrual/Yr
Thyroid	11.5/million	863	17
Melanoma	2-5/million	150-375	8
Retinoblastoma	2-5/million	150-375	29
Neuroendocrine Tumors	2.8/million	210	12
NPC	1/million	75	9
Colorectal	1/million	75	3
Desmoplastic Small Round Cell Tumors	0.5/million	38	6
Gonadal Stromal Tumors	<0.5/million	<38	11
<u>Pancreatoblastoma</u>	<0.25/million	19	<1
Pleuropulmonary Blastoma	<0.25/million	19	5
ACC	0.21/million	16	4
Gastrointestinal Stromal Tumors	0.02-0.11/million	2-9	2

Regulatory Rare Cancer Efforts

- **FDA guidance:** Rare tumor natural history studies, external controls, real world data
- **Regulatory approvals for very rare cancers pediatric and adult:**

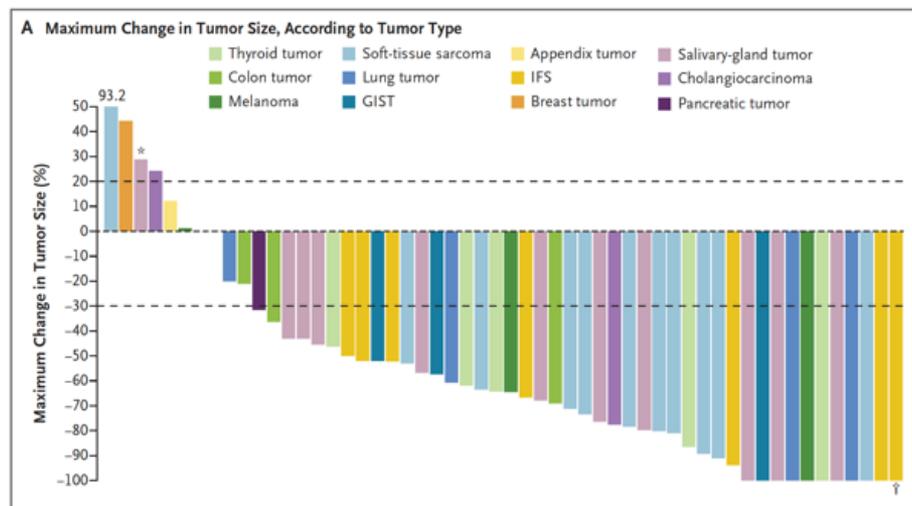
Atezolizumab: Alveolar soft part sarcoma

- ≥ 2 years old
- ORR 24%, DOR ≥ 12 months 42%
- 47 adult, 2 pediatric patients

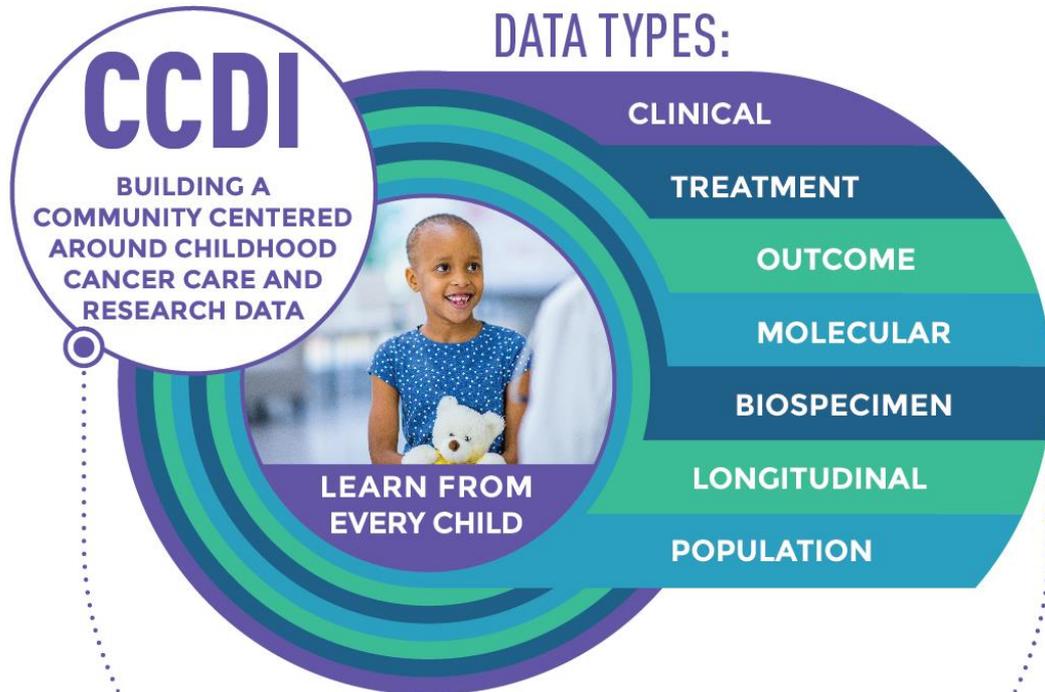


Larotrectinib: NTRK gene fusion cancers

- Pediatric and adult patients, histology agnostic
- ORR 75%, DOR ≥ 9 months 63%
- 43 adult, 12 pediatric patients



Pediatric Data Efforts: NCI Childhood Cancer Data Initiative (CCDI)



Improving the quality, consistency, and accessibility of data to make it easier for researchers to develop new and better treatments for children with cancer.

Learn from and use data:

- EHR pilots
- Cohorts
- Survivorship
- Data catalog

Aggregate and generate data:

- Preclinical models
- Molecular characterization
- Rare tumor initiative

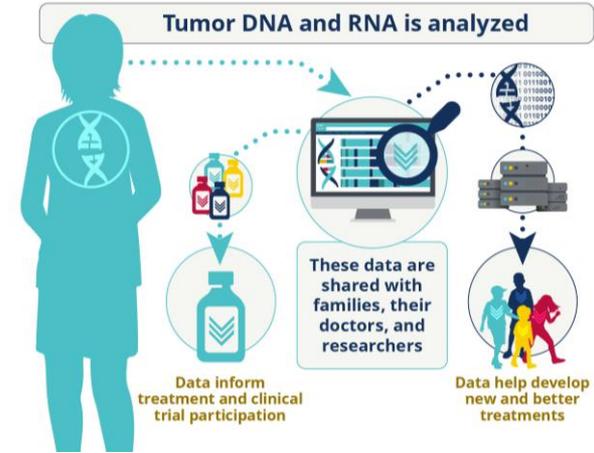
Build foundational infrastructure:

- Data ecosystem
- CCDI participant index
- Computable consent
- Tools interoperability
- Federated infrastructure
- Clinical data commons

CCDI Molecular Characterization Initiative (MCI)

- Partnership between NCI and COG Project:EveryChild
- State-of-the-art molecular characterization at diagnosis
 - WES, fusions, methylation
- Results returned to participants and treating physicians within 21 days
- Remaining samples will be stored in a biobank for future research
- Identification of molecular tumor subtypes

In its first year, MCI enrolled more than 1,000 participants from 47 states, Canada, Australia, and New Zealand.



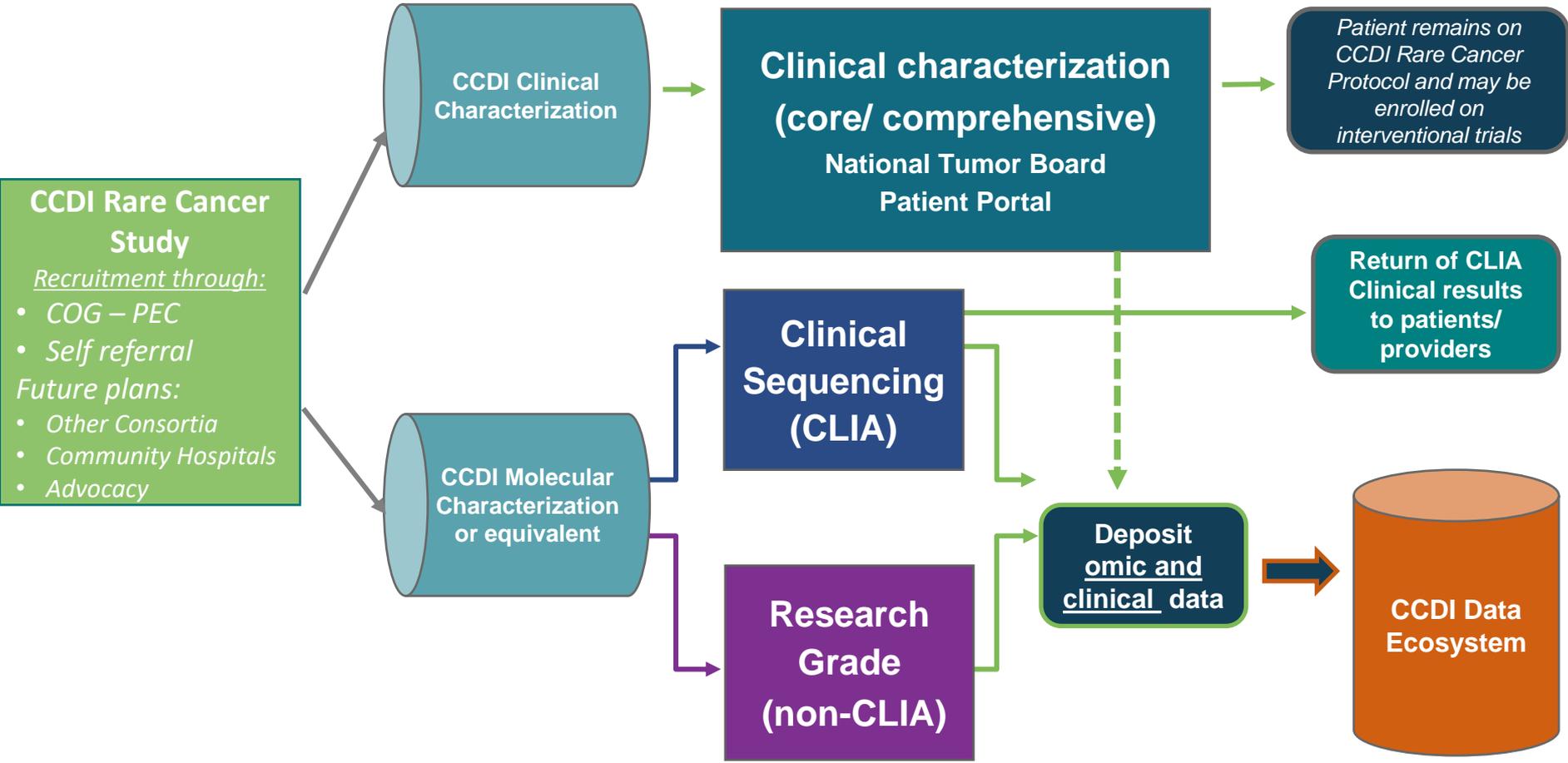
Lessons Learned and Path Forward

- Successful efforts have: Advocacy, patient engagement, and disease champions
- Conducting registry/natural history studies facilitates clinical trials
- Broad collaboration engaging multiple stakeholders critical
- **A national/international effort will allow enrolling adequate numbers of participants to more rapidly, efficiently, and consistently study multiple rare cancers**
- CCDI rare cancer workshop (November 2022, virtual)
 - Discuss framework and seek support
- CCDI symposium (March 2023, in person and virtual):
 - Present and discuss rare cancer effort
 - Breakout sessions for direct feedback
- CCDI task force meetings to develop consensus for:
 - Clinical core elements, rare tumors for pilot approach, protocol development

Objectives

- Feasibility of a national observational protocol for very rare pediatric and AYA solid cancers and hematologic malignancies
- Longitudinally evaluate the disease course of participants with rare cancers
 - Structured and real world data
 - External control for interventional trials
 - Meaningful comparison across multiple cancer types
- Collect clinical and research molecular characterization
 - Identification of therapeutic targets and inform clinical trials
- Feasibility of national molecular/clinical tumor boards for rare cancers
 - Facilitation of patient navigation and treatment recommendations

NCI CCDI-Coordinated Rare Pediatric/AYA Cancer Study



European Union Collaboration Opportunities

Data collection:

- Substantially increase number of patients with very rare cancers for analysis
 - Identical clinical core data for rare tumors
 - Make utility of CCDI resources, tools, data ecosystem
- Building external control for clinical trials
- Streamlined molecular characterization

Molecular tumor boards:

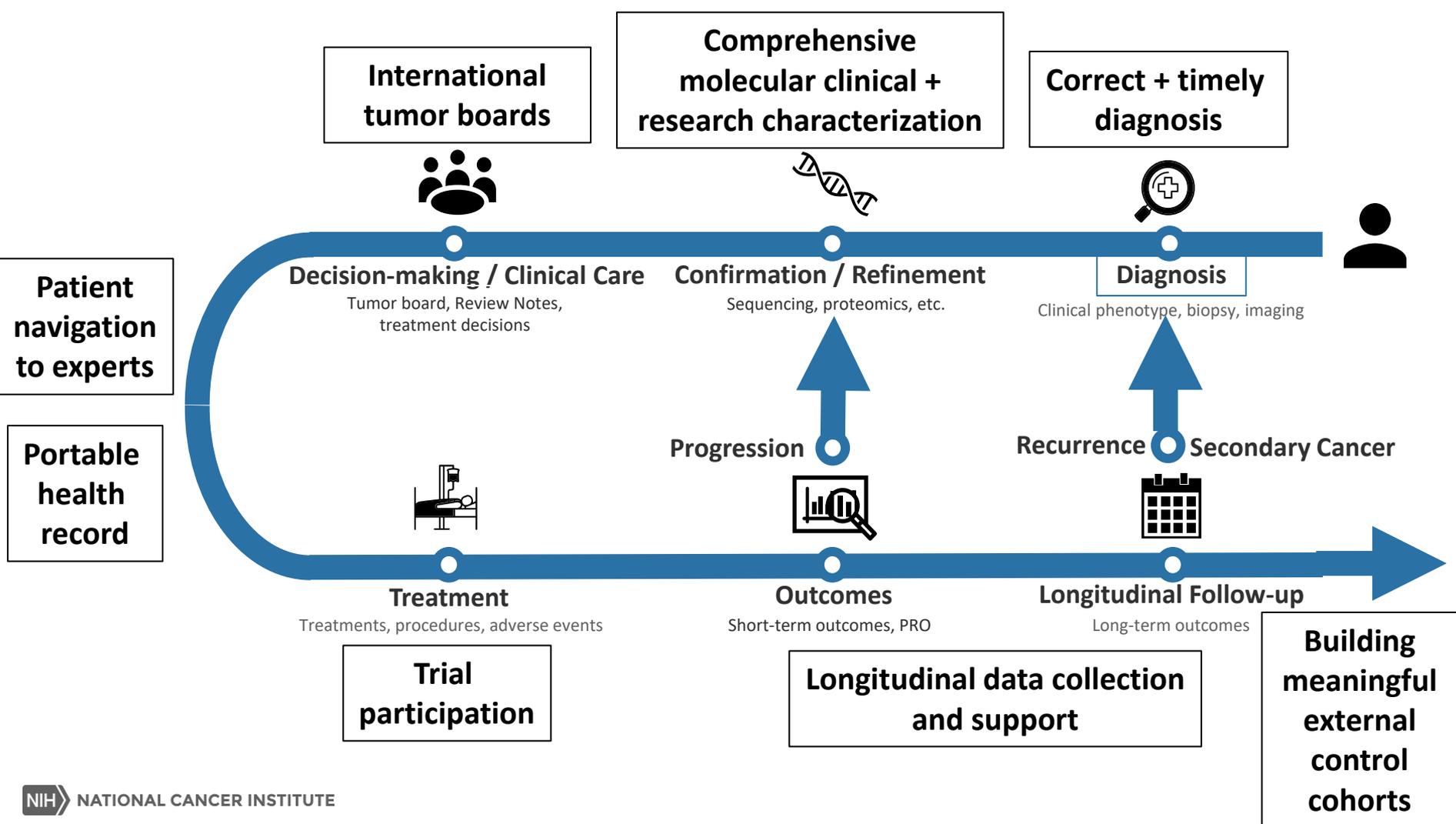
- International representation for virtual rare tumor boards (disease champions)

Evidence based recommendations for evaluation and management of rare cancers

Interventional clinical trials:

- In collaboration with FDA/EMA, consortia and industry

EU Co-Chair: Dr. Ruth Ladenstein, Deputy Director, Children's Cancer Research Institute, Vienna, Austria



International tumor boards

Comprehensive molecular clinical + research characterization

Correct + timely diagnosis

Patient navigation to experts

Portable health record

Decision-making / Clinical Care
Tumor board, Review Notes, treatment decisions

Confirmation / Refinement
Sequencing, proteomics, etc.

Diagnosis

Clinical phenotype, biopsy, imaging

Treatment

Treatments, procedures, adverse events

Trial participation

Outcomes

Short-term outcomes, PRO

Longitudinal data collection and support

Longitudinal Follow-up

Long-term outcomes

Building meaningful external control cohorts

Progression

Recurrence Secondary Cancer

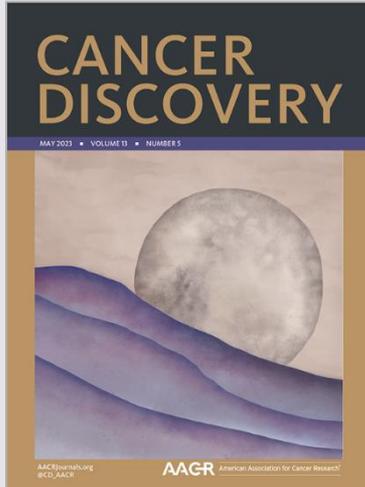
If you work on frequent cancers: Do randomized trials
If you work on rare cancers: **FIND FRIENDS**

Shared opportunities for reducing lung cancer mortality in the US and EU

*Neal Freedman, Ph.D.
Tobacco Control Research Branch*



Reduce **age-standardized** cancer mortality rates by at least 50% over the next 25 years

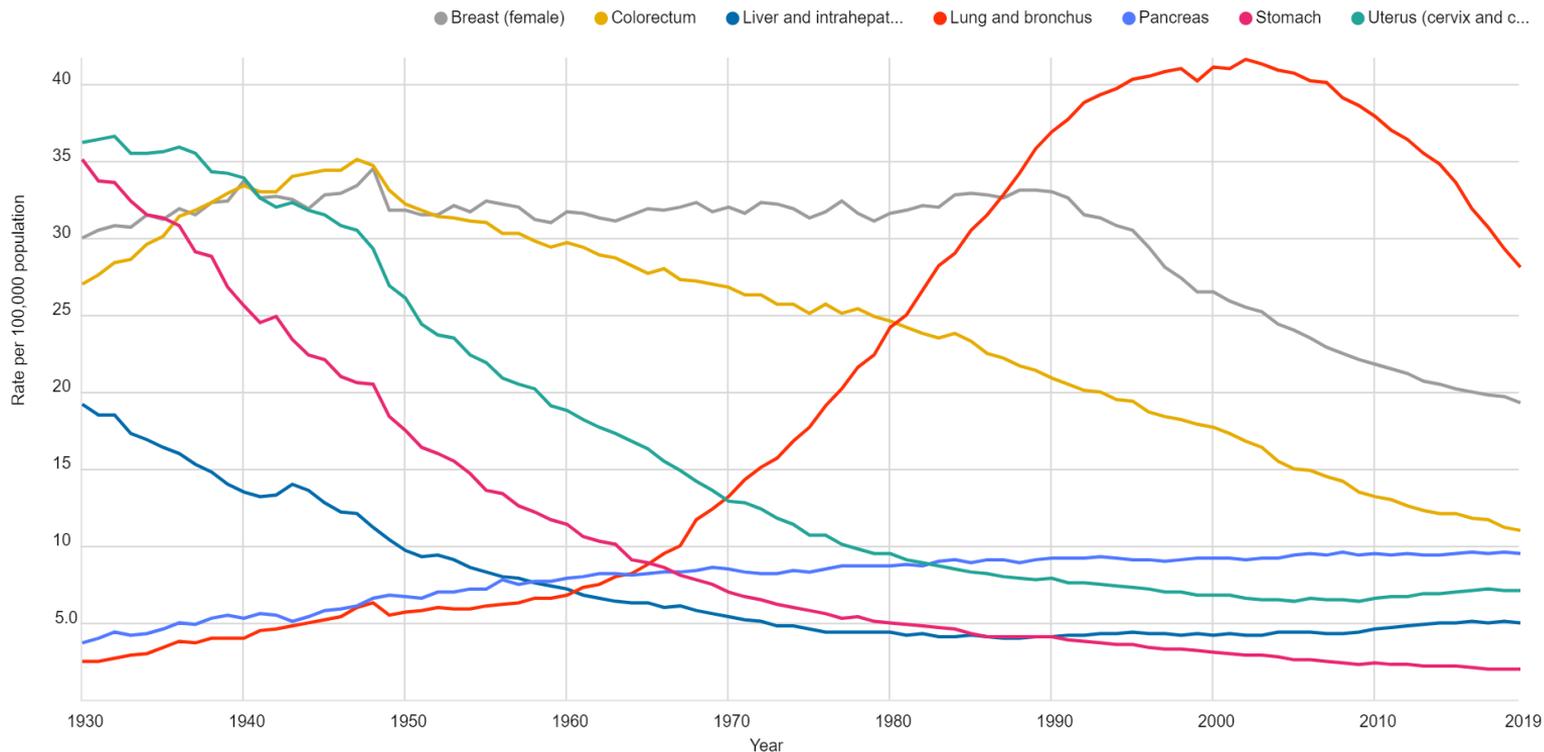


Opportunities for Achieving the Cancer Moonshot Goal of a 50% Reduction in Cancer Mortality by 2047

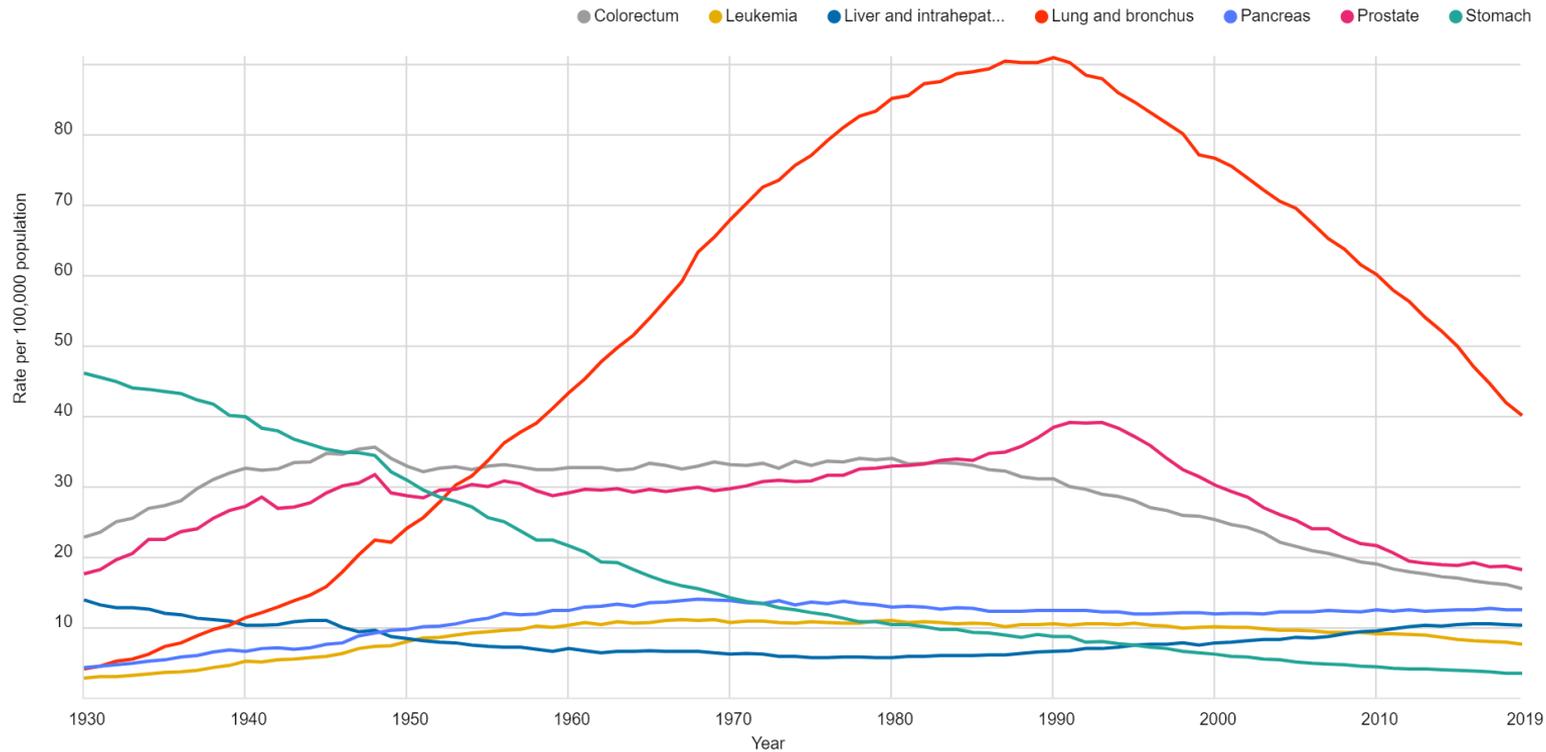
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Rates of cancer mortality in US women, 1930-2019



Rates of cancer mortality in US men, 1930-2019

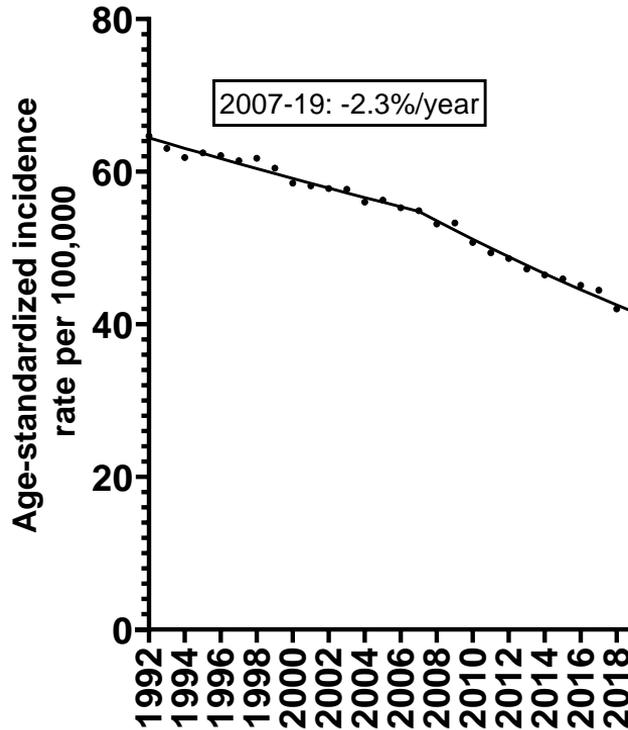


Most common causes of cancer death in the US, 2019

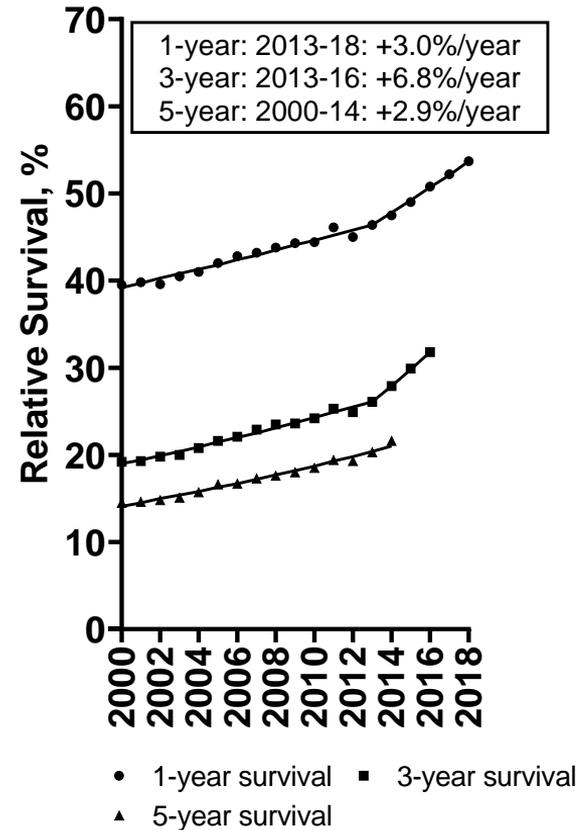
Cancer site	Deaths	% of deaths
Lung	139,601	23.3%
Colorectal	51,896	8.7%
Pancreas	45,885	7.7%
Female Breast	42,280	7.1%
Prostate	31,636	5.3%
Liver	27,958	4.7%

Lung Cancer

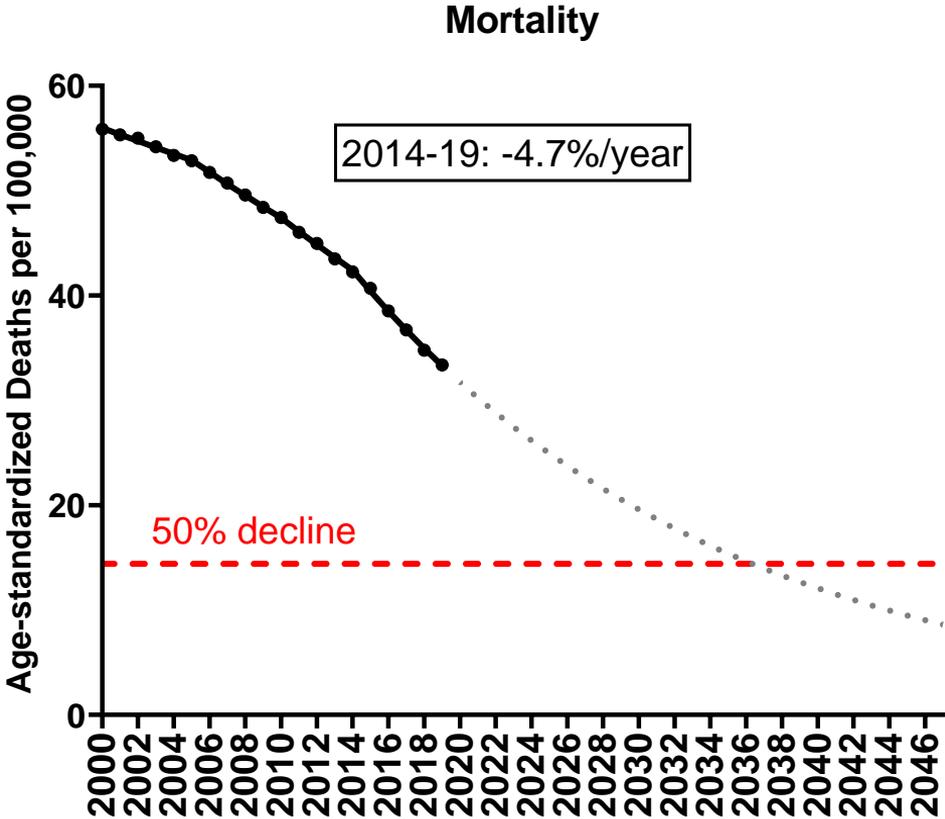
Incidence



Survival



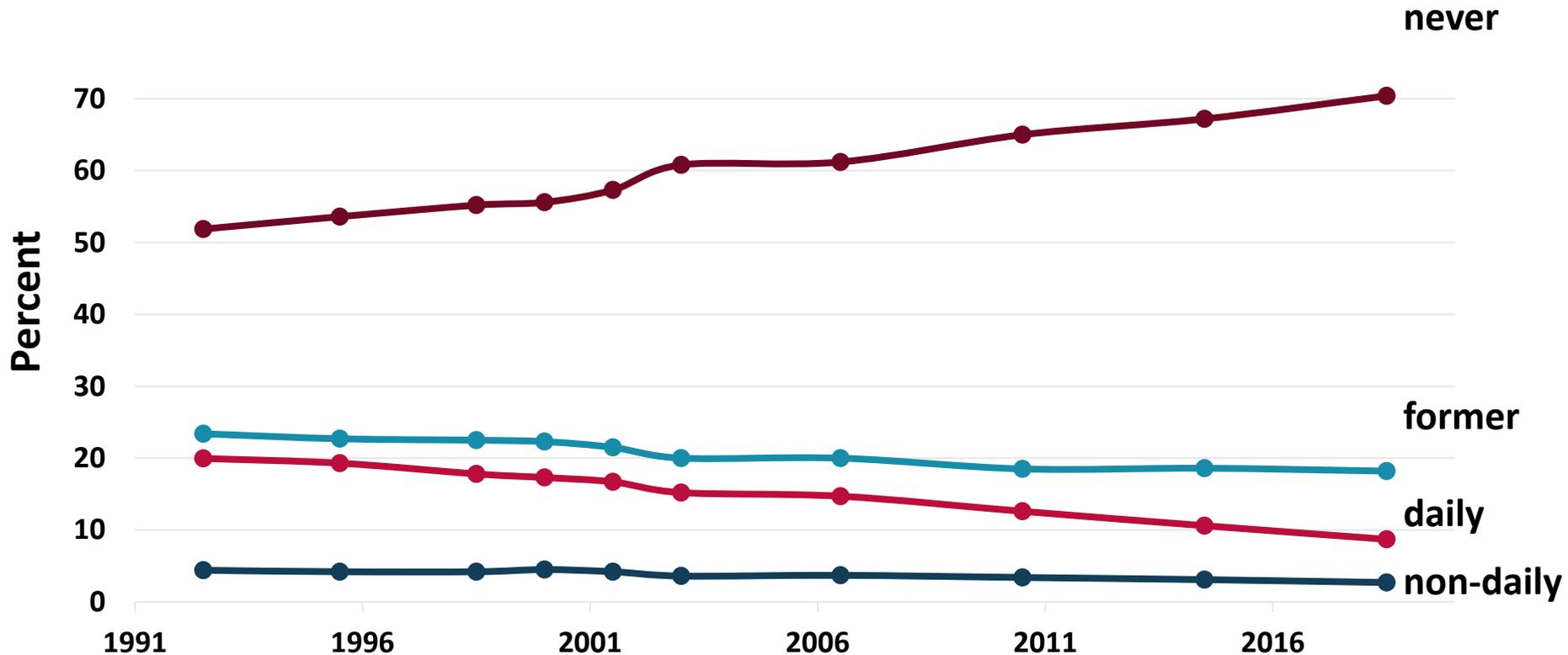
Lung Cancer



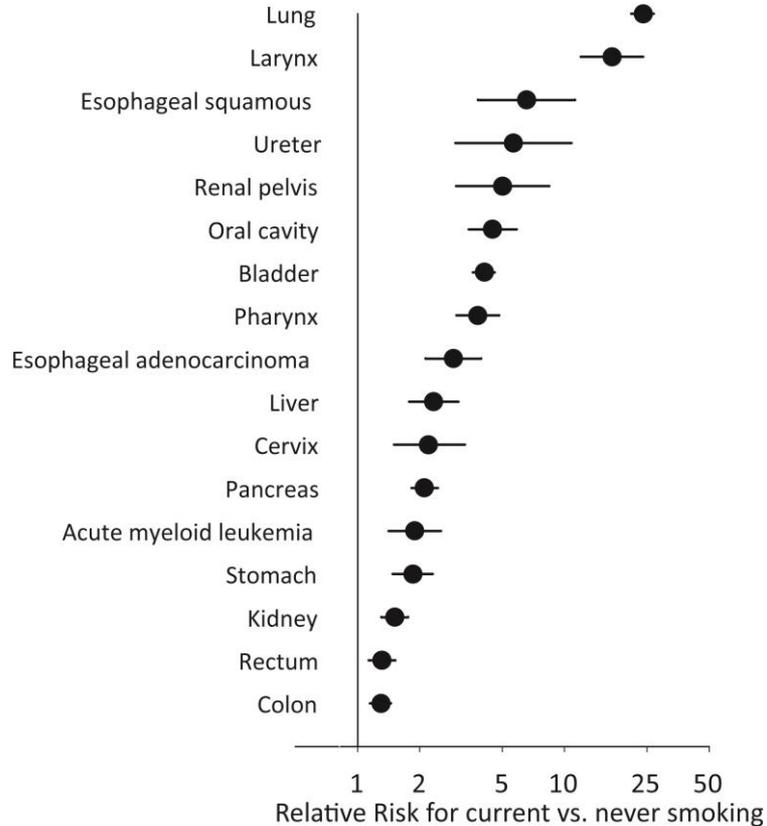
Lung Cancer

Outcome	Potential intervention type	Opportunity?
Incidence	Lifestyle factors	Increase smoking cessation; prevent initiation
Mortality	Screening (Early detection)	Increase low-dose CT uptake and reduce disparities in use
	Treatment	Reduce disparities in access to more effective treatments (targeted and immune-based therapies for NSCLC)

Smoking prevalence in the U.S.

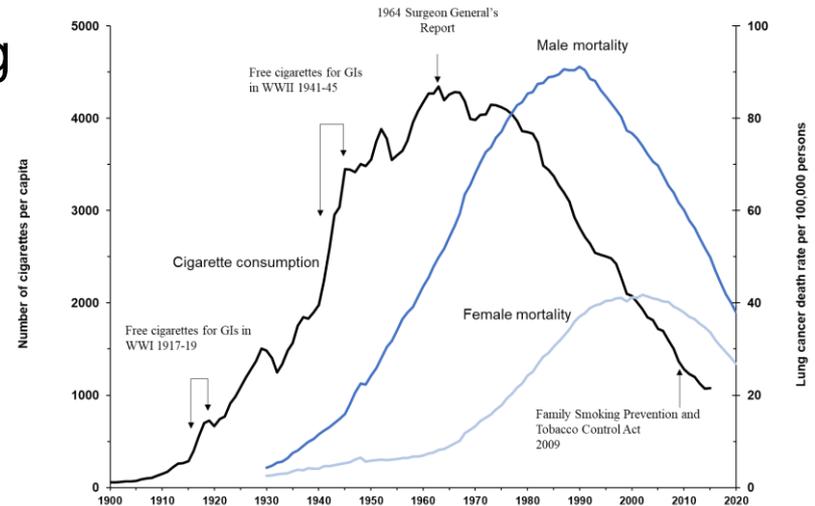


Smoking causes many cancer types



Continued declines in lung cancer expected

- Progress in smoking declines from recent years has not yet impacted lung cancer death rates
- 2% of high school students reported smoking in 2022
- FDA-CTP announcements regarding proposed tobacco product standards
 - Prohibiting menthol
 - Reducing nicotine



ACS Cancer Facts & Figures, 2023

Many disparities in cigarette smoking remain

Prevalence of cigarette smoking by Education in adults, 2020 (NHIS)	
0-12 years (no diploma)	21.5%
GED	32.0%
High School diploma	17.6%
Associate Degree	12.7%
Bachelor's degree	5.6%
Graduate degree	3.5%

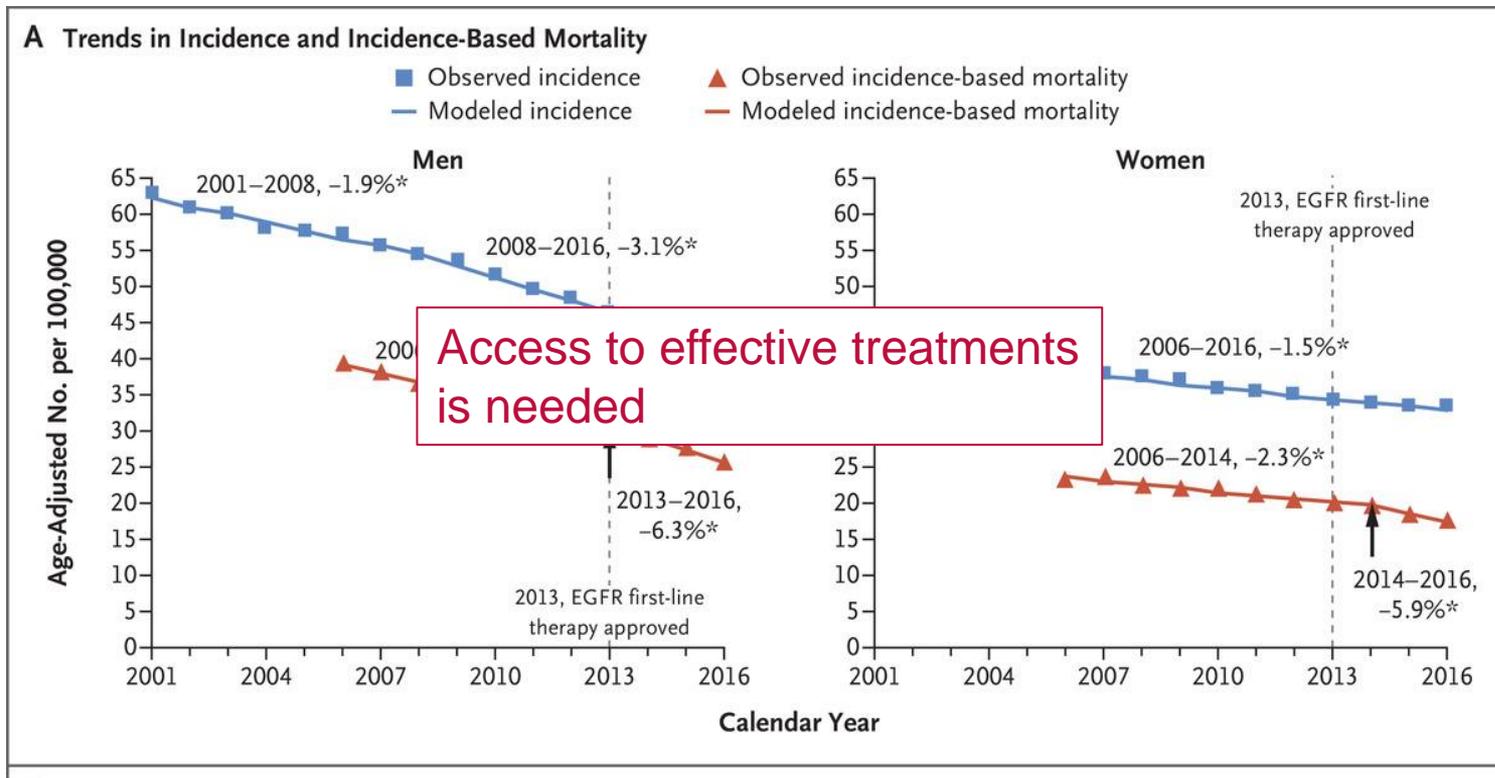
Cornelius et al, MMWR, 2022

Non-small cell lung cancer (NSCLC) treatments improved survival

¾ of lung cancer cases in the U.S.

Targeted therapies against oncogenic driver mutations and immune-based therapies have contributed to population-level declines in lung cancer mortality

NSCLC treatments improved survival



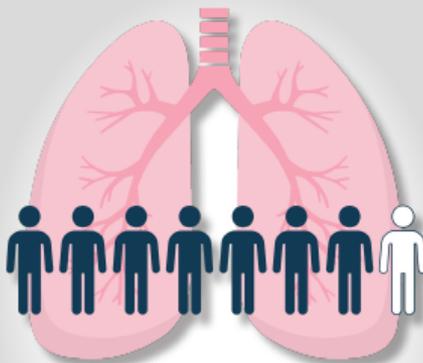
LUNG CANCER SCREENING SAVES LIVES

Lung Cancer is #1 Cause of Cancer Deaths



Screening with low dose CT* can detect lung cancer early and save lives

More Screening is Needed



7 of **8** adults who met **screening criteria** did not report recommended screening

Healthcare Providers: Discuss Screening



With Adults

- ✓ Age 55–80
- ✓ Heavy smoking history**
- ✓ Smoke now or quit within the past 15 years

*Low-dose computed tomography (CT) is the only test recommended by the US Preventive Services Task Force.

**Heavy smoking is a smoking history of 30 pack-years or more. A pack-year is smoking an average of one pack of cigarettes per day for one year.

Data from BRFSS, 10 states in 2017, as reported in Richards et al, *MMWR* 2020 Read the full report: bit.ly/CDCVA34

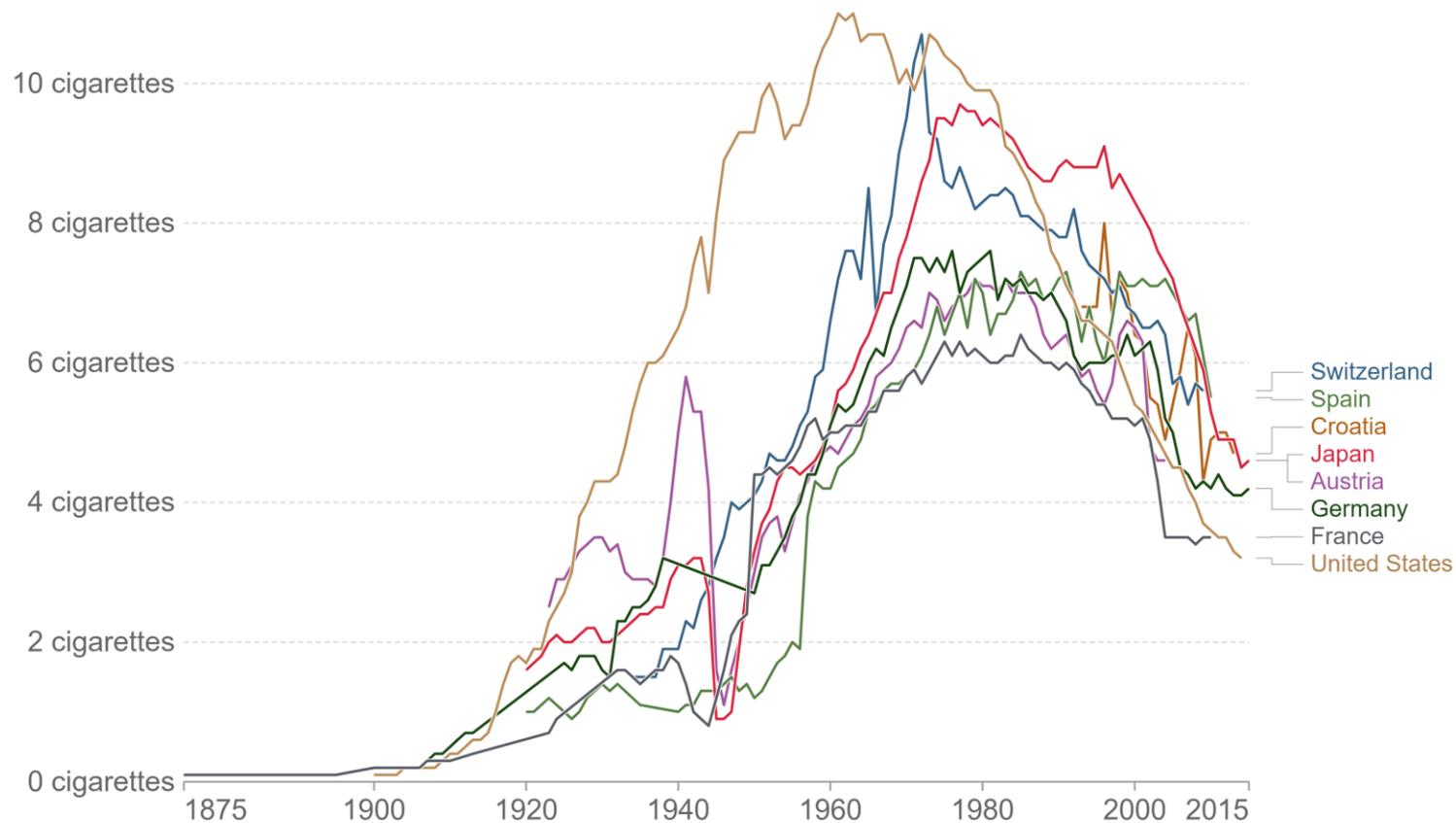
Most common causes of cancer death in the EU, 2020

Cancer site	Deaths	% of deaths
Lung	257,293	20.4%
Colorectal	156,105	12.4%
Breast	91,826	7.3%
Pancreas	89,256	7.1%
Prostate	69,945	5.5%
Liver	53,869	4.3%

<https://ecis.jrc.ec.europa.eu/>

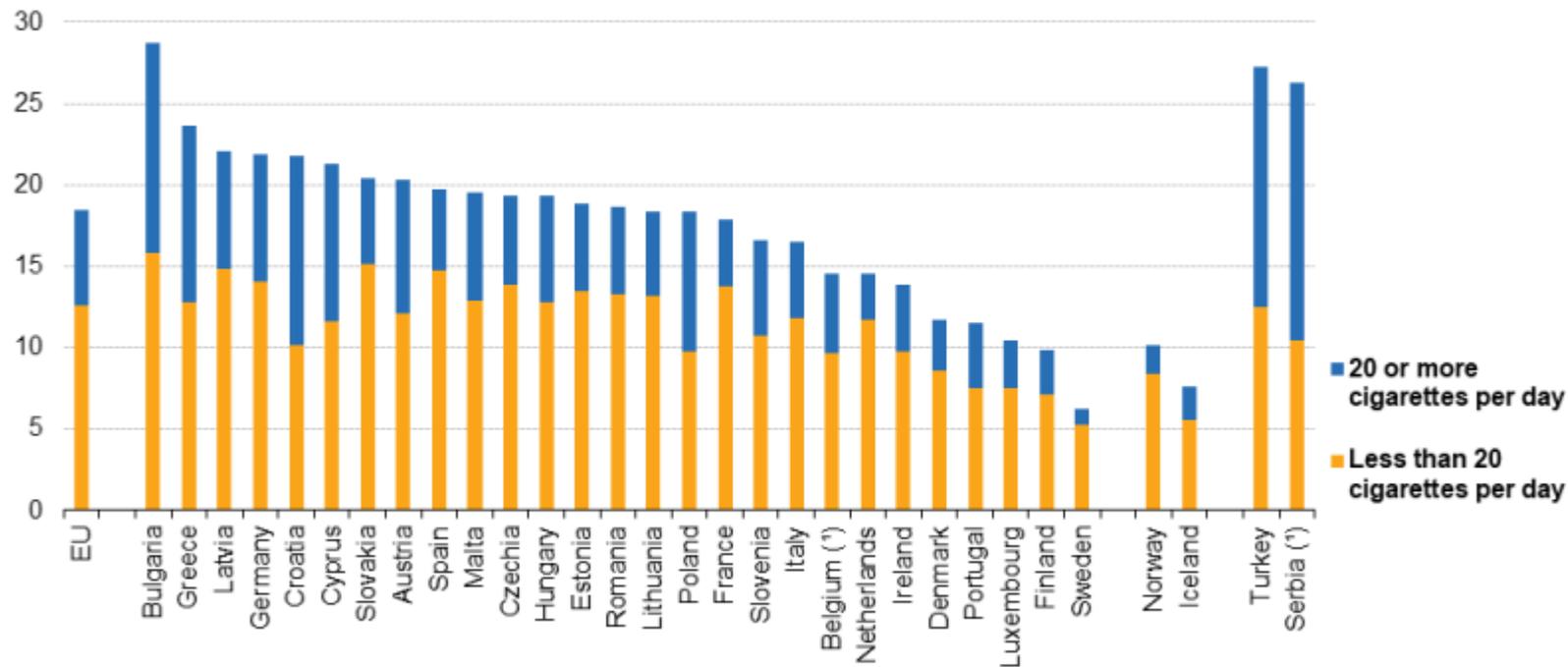
Sales of cigarettes per adult per day, 1875 to 2015

Figures include manufactured cigarettes, as well as estimated number of hand-rolled cigarettes, per adult (ages 15+) per day.



Share of daily smokers of cigarettes among persons aged 15 and over, by level of consumption, 2019

(%)



Note: ranked on the share of all daily smokers.

(*) Low reliability.

Source: Eurostat (online data code: hlth_ehis_sk3e)

European Union Collaboration Opportunities

Co-chair: Professor Harry de Koning (Erasmus, PI: NELSON trial)

Build on prior efforts and strengths, eg

WH Cancer Moonshot Smoking Cessation Forum (June 1, 2023)

[\(White House Cancer Moonshot Forum on Smoking Cessation – YouTube\)](#)

NLST (National Lung Screening Trial)

CISNET Lung (Cancer Intervention and Surveillance Modeling Network)

C3I (Cancer Center Cessation Initiative)

PROSPR Lung (Population-based Research to Optimize the Screening Process)

SCALE (Smoking Cessation at Lung Examination)